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We claim:

1 1. A method for inducing a cellular immune response to a non-immunogenic or weakly
2 immunogenic-target peptide expressed by tumor cells of a mammalian subject,
3 6/12/99 ✓ comprising administering to the mammalian subject an amount of a therapeutic
4 antigen effective to induce a cellular immune response to the target peptide, wherein
5 the therapeutic antigen comprises an immunogenic portion having an MHC-binding
6 domain which binds to the major histocompatibility complex (MHC) and an immune-
7 recognition domain which is recognized by T-cells, and wherein the therapeutic
8 antigen is derived from the target peptide such that the MHC-binding portion binds to
9 MHC with a greater affinity than the target peptide without material alteration of the
10 immune-recognition portion.

1 2. The method of claim 1, wherein the target peptide and the immunogenic portion of the
2 therapeutic antigen each consist of from 8 to 14 amino acids. 6/11/99

1 3. The method of claim 1, wherein the therapeutic antigen further comprises a sorting
2 signal for directing trafficking of the therapeutic antigen to the endoplasmic reticulum.
3

1 4. ~~The method of claim 2, wherein the target peptide and the immunogenic portion of the~~
2 ~~therapeutic antigen each consist of from 8 to 14 amino acids.~~ 5/15/99

1 5. ~~The method of claim 1, wherein the therapeutic antigen is administered by~~
2 ~~administration of a nucleic acid encoding the therapeutic antigen, which nucleic acid~~
3 ~~is expressed in the mammalian subject.~~

1 6. ~~The method of claim 5, wherein the target peptide and the immunogenic portion of the~~
2 ~~therapeutic antigen each consist of from 8 to 14 amino acids.~~

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7. The method of claim 1, wherein the therapeutic antigen further comprises a sorting signal for directing trafficking of the therapeutic antigen to the endoplasmic reticulum or endosomes.
8. The method of claim 7, wherein the target peptide and the immunogenic portion of the therapeutic antigen each consist of from 8 to 14 amino acids. 611199
9. The method of claim 1, wherein the MHC-binding domain binds to an MHC Class I molecule and the immune-recognition domain binds to a cytotoxic T cell.
- ~~10.~~ The method of claim 1, wherein the MHC-binding domain binds to an MHC Class II molecule and the immune-recognition domain binds to a CD4+ T cell.
11. The method of ~~any of claims 1 to 8,~~^{claim 1} wherein the target peptide binds to HLA-A* 0201.
12. The method of ~~any of claims 1 to 10,~~^{claim 1} wherein the target peptide is a self-peptide expressed in normal and tumor tissues of the mammalian subject.
13. The method of claim 12, wherein the target peptide derived from is gp75.
14. The method according to claim 13, wherein the therapeutic antigen has the sequence TAYRYHLL (Seq. ID No. 12).
- ~~15.~~ The method of claim 12, wherein the target peptide is selected from the group consisting of telomerase reverse transcriptase peptide, CD20 peptides and Prostate PSMA peptide. 611199
16. The method of ~~any of claims 1 to 10,~~^{claim 1} wherein the target peptide is a Herpes simplex glycoprotein B peptide and the therapeutic antigen is SSIEFARL (Seq. ID No. 10).

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1 17. A method for preparation of a vaccine against a non-immunogenic or weakly
2 immunogenic target protein expressed by tumor cells of a mammalian subject,
3 comprising the steps of:

4 (a) identifying an 8-14 amino acid target peptide within the target protein,
5 said target peptide including an MHC-binding domain which binds with low affinity to the
6 major histocompatibility complex (MHC) and an immune-recognition domain which is
7 recognizable by T-cells;

8 (b) preparing one or more test peptides in which the MHC binding domain
9 is modified and testing the test peptide for binding affinity to the MHC;

10 (c) selecting a test peptide from among the one or more test peptides for
11 use in the vaccine, said selected peptide having a greater binding affinity than the target
12 peptide; and

13 (d) preparing a vaccine composition comprising the selected peptide or a
14 polynucleotide encoding the selected peptide in a pharmaceutically acceptable carrier.

15 18. The method of claim 17, wherein the target peptide binds to HLA-A* 0201.

16 19. The method of claim 17, further comprising the step of coupling the selected peptide
17 with a sorting signal for directing trafficking of the therapeutic antigen to the
18 endoplasmic reticulum or endosomes.

19 20. The method of claim 17, wherein the MHC-binding domain binds to an MHC Class I
20 molecule and the immune-recognition domain binds to a cytotoxic T cell.

21 21. The method of claim 17, wherein the MHC-binding domain binds to an MHC Class II
22 molecule and the immune-recognition domain binds to a CD4+ T cell.

23 ^{claim 17}
24 22. The method of ~~any of claims 17-21~~, wherein the target protein is a self-protein
25 expressed in normal and tumor tissues of the mammalian subject.

26 ^{claim 17}
27 23. The method of ~~any of claims 17-21~~, wherein the target peptide derived from is gp75.

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claim 17

- 1 24. The method of ~~any of claims 17-21~~, wherein the target peptide is selected from the
2 group consisting of telomerase reverse transcriptase peptide, CD20 peptides and
3 Prostate PSMA peptide.

claim 17

- 1 25. The method of ~~any of claims 17-21~~, wherein the therapeutic antigen has the sequence
2 TAYRYHLL (Seq. ID No. 12).

claim 17

- 1 26. The method of ~~any of claims 17-21~~, wherein the target peptide is a Herpes simplex
2 glycoprotein B peptide and the therapeutic antigen is SSIEFARL (Seq. ID No. 10).

- 1 27. A therapeutic immunogen comprising an MHC-binding domain which binds to the
2 major histocompatibility complex (MHC) of a mammalian subject and an immune-
3 recognition domain which is recognized by T-cells. wherein the therapeutic
4 immunogen is derived from a non-immunogenic or weakly immunogenic target
5 peptide expressed by tumor cells of the mammalian subject such that the MHC-
6 binding portion binds to MHC with a greater affinity than the target peptide without
7 material alteration of the immune-recognition portion.

- 1 28. The therapeutic immunogen of claim 27, further comprising a sorting signal for
2 directing trafficking of the therapeutic antigen to the endoplasmic reticulum or
3 endosomes.

- 1 29. The therapeutic immunogen of claim 27, wherein the MHC-binding domain binds to
2 an MHC Class I molecule and the immune-recognition domain binds to a cytotoxic T
3 cell.

- 1 30. The therapeutic immunogen of claim 27, wherein the MHC-binding domain binds to
2 an MHC Class II molecule and the immune-recognition domain binds to a CD4+ T
3 cell.

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1 31. A polynucleotide expressible in a mammalian subject, comprising a series of bases
2 encoding the therapeutic immunogen of ~~any of claims claim 27 to 30.~~ ^{claim 27}

1 32. A vaccine composition for treatment or prevention of a tumor in a mammalian
2 subject, comprising a therapeutic immunogen in accordance with ~~any of claims claim~~ ^{claim 27}
3 ~~27 to 30,~~ or a polynucleotide expressible in the mammalian subject comprising a
4 series of bases encoding the therapeutic immunogen of any of claims claim 27 to 30,
5 together with a pharmaceutically acceptable carrier.

1 33. The composition according to claim 32, wherein the pharmaceutically acceptable
2 carrier comprises an adjuvant.